

**REMARKS**

**I. Support for Amendments to the Claims**

The amendments to the claims finds support at page 8-9 and elsewhere in the specification specification.

**II. Sequence Compliance**

Applicants respectfully request that sequence compliance formalities be held in abeyance until the application is in condition for allowance.

**III. Specification**

Applicants thank the Examiner for renumbering the claims and apologize for the error in mis-numbering claims 30-46.

**IV. Claim Objections**

Claim 33 was objected to as depending from a non-elected claim. Claim 33 has been amended but respectfully note that it did not depend on any other claim.

**V. Claim Rejections 35 USC §101**

Claims 21 and 22 were rejected as being directed to non-statutory subject matter. Claims 21-22 have been cancelled.

**VI. Rejection under 35 U.S.C. §112, second paragraph –failure to particularly point out and claim**

The Examiner has rejected Claims 21-22 as being indefinite for depending from a non-elected claim. Claims 21 and 22 have been cancelled.

The Examiner has rejected claims 23-33 as being indefinite because claims 23-33 are drawn to:

[A]n enzyme labeled as heparanase II. It is not clear to the Examiner as to how one skilled in the art will be able to distinguish “heparanase II” from other human heparanase already disclosed in the prior art. A perusal of the specification does not provide a specific or distinguishing assay based on which the instant enzyme can be identified as “heparanase II.” The only information that is provided is that the instant enzyme has an amino acid sequence that is different from that already disclosed in the prior art. Therefore, it is not clear to the Examiner

as to whether the instant is a simple variant of the already known heparanase or an entirely different class of heparanase as to how those skilled in the art can identify the above protein without first analyzing its amino acid sequence.

The Examiner notes on the record:

[That] [t]he only information that is provided is that the instant enzyme has an amino acid sequence that is different from that already disclosed in the prior art.

Solely in order to expedite prosecution, Applicants have amended the claims to eliminate reference to "heparanase II" but would like to point out that the term "heparanase II" is fully defined within the specification at page 8, lines 19-26. Specifically a "heparanase II polypeptide" is defined in relation to **SEQ ID NO:2**. The differences between SEQ ID NO:2 and the sequence art recognized as being designated heparanase I are self evident from the sequence comparison set forth in Figure 2. It is well within the scope of the abilities of one of ordinary skill to distinguish two proteins having different amino acid sequences but the same enzymatic activity. By way of non-limiting example, the specification teaches specific primers which are capable of amplifying nucleic acids encoding heparanase II and not prior art sequences at page 35 through 36 of the specification and antibodies capable of distinguishing heparanase II from prior art sequences. Determining the sequence of a protein is also a technique well known in the art. Therefore it is Applicant's position that their amendment of the claims is not a narrowing amendment and no narrowing is intended by their amendment.

The Examiner notes:

It is not clear to the Examiner as how two fragments cleaved from a single enzyme with a single catalytic region continues to be active even after their separation. It is not clear whether the above enzyme has two catalytic sites both of which equally active when residing in a single polypeptide. A perusal of the specification does not provide any such characteristics of the enzyme except for the identification of the signal peptide sequence.

Applicants respectfully point out that the issue of enzymatic activity is irrelevant to

whether they have distinctly pointed out and claimed their invention. Applicants would point the Examiner to *Ex parte Wu*:

In rejecting a claim under the second paragraph of 35 USC 112, it is incumbent on the examiner to establish that one of ordinary skill in the pertinent art, when reading the claims in light of the supporting specification, would not have been able to ascertain with a reasonable degree of precision and particularity the particular area set out and circumscribed by the claims. *Ex parte Wu*, 10 USPQ 2d 2031, 2033 (B.P.A.I. 1989)

Applicants are at a loss to determine how they might more definitely claim a sequence than by reference to residue number and SEQ ID NO. and would point out that *Wu* does not require more. Applicants would also point the Examiner to Fairbanks *et al.* J. Biol. Chem. 274(42):29587-90, 1999. (Considered by the Examiner on 5-14-03 and provided with Applicant's Form 1449 and referenced and discussed in Example 2, page 39) which should allay the Examiner's confusion. The Example explains that heparanase enzymes are art recognized as being subject to cellular processing. Further explanation is found in the Summary of the Invention at page 8-9.

## VII. Rejection of the Claims under 35 USC § 112—Enablement

The Examiner has rejected claims 21, 22, 23 (parts c-f), 26, 27, 28, 29 and 33 as being nonenabled presumably because the claims are not limited to sequences derived from SEQ ID NO:2 and that the claims are "so broad as to encompass any or all human heparanases".

As noted above the Applicants respectfully disagree but note that to the extent the Examiner is objecting to the recitation of "heparanase II" the Examiner's concern is rendered moot by the amendment of the claim and once again note that they are not intending to narrow the scope of the claims.

The Examiner states:

While recombinant and mutagenesis techniques are known, *it is not routine in the art to screen* for large numbers of variants, mutants or fragments as encompassed by the instant claims .... and the result of such modifications are unpredictable. [emphasis added]

The Examiner grossly misstates the law. The Federal Circuit has specifically validated the proposition that a disclosure that utilizes routine screening using well known procedures to make the invention constitutes an enabling disclosure.

With respect to screening, the only permissible view of the evidence is that screening methods used to identify the necessary characteristics, including affinity, of the monoclonal antibodies used in the invention were known in the art and that the '110 patent contemplated one of those. At trial, Monoclonal's counsel stated "it is a procedure that was known in '78." . . . We hold as a matter of law that the '110 patent disclosure is enabling.

Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 U.S.P.Q. (BNA) 81 (Fed. Cir. 1986)

If the Examiner is aware of Hybritech being overruled or only applying to the field of monoclonal antibodies, Applicants respectfully request that the Examiner make such authority of record in this case.

### **VIII. Claim Rejections—35 USC § 102**

Claims 21-22 were rejected as allegedly being anticipated by Freeman et al. (1998). The claims have been cancelled thereby rendering the rejection moot.

Claims 21-23, 26-27 and 33 were rejected under 35 USC 102(e) as being anticipated by Fiscella et al. WO 01/79253 with an apparent effective US filing date of April 18, 2000. Applicants submit that the Fiscella may be antedated as it is not a US patent or US patent application publication. Without in any way acquiescing in the Examiner's characterization of Fiscella, Applicants submit a declaration indicating that the invention was made prior to the effective date of Fiscella thereby rendering the Examiners rejection moot. The attached Exhibit indicates that the Applicants had conceived of their invention before the apparent effective date of Fiscella. Certain portions of the Exhibit have been redacted in accord with standard patent practice.

### **IX. Conclusion**

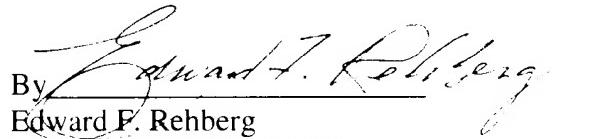
In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully

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requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

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Respectfully submitted,

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